Efficient Generation of Hematopoietic Precursors and Progenitors From Human Pluripotent Stem Cell Lines.

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Public Summary:
By mimicking embryonic development of the hematopoietic system, we have developed an optimized in vitro differentiation protocol for the generation of precursors of hematopoietic lineages and primitive hematopoietic cells from human embryonic stem cells (ES) and induced pluripotent stem cells (iPS). Factors such as cytokines, extra cellular matrix components, and small molecules, as well as the temporal association and concentration of these factors were tested on seven different human ES and iPS lines. We report the differentiation of up to 84% huCD45+ cells (average 41% +/- 16, from 7 pluripotent lines) from the differentiation culture, including significant numbers of primitive CD45+/CD34+ and CD45+/CD34+/CD38- hematopoietic progenitors. Moreover, the numbers of hematopoietic progenitor cells generated, as measured by colony forming unit assays were comparable to numbers obtained from fresh umbilical cord blood mononuclear cell isolates on a per CD45+ cell basis. Our approach demonstrates highly efficient generation of multipotent hematopoietic progenitors with the highest efficiencies reported to date (CD45+/CD34+) using a single standardized differentiation protocol on several human ES and iPS lines. Our data add to the cumulating evidence for the existence of an in vitro derived precursor to the hematopoietic stem cell (HSC) with limited engrafting ability in transplanted mice, but with multipotent hematopoietic potential. Because this protocol efficiently expands the pre-blood precursors and hematopoietic progenitors, it is ideal for testing novel factors for the generation and expansion of definitive HSCs with long-term repopulating ability.

Scientific Abstract:
By mimicking embryonic development of the hematopoietic system, we have developed an optimized in vitro differentiation protocol for the generation of precursors of hematopoietic lineages and primitive hematopoietic cells from human embryonic stem cells (ES) and induced pluripotent stem cells (iPS). Factors such as cytokines, extra cellular matrix components, and small molecules, as well as the temporal association and concentration of these factors were tested on seven different human ES and iPS lines. We report the differentiation of up to 84% huCD45+ cells (average 41% +/- 16, from 7 pluripotent lines) from the differentiation culture, including significant numbers of primitive CD45+/CD34+ and CD45+/CD34+/CD38- hematopoietic progenitors. Moreover, the numbers of hematopoietic progenitor cells generated, as measured by colony forming unit assays were comparable to numbers obtained from fresh umbilical cord blood mononuclear cell isolates on a per CD45+ cell basis. Our approach demonstrates highly efficient generation of multipotent hematopoietic progenitors with the highest efficiencies reported to date (CD45+/CD34+) using a single standardized differentiation protocol on several human ES and iPS lines. Our data add to the cumulating evidence for the existence of an in vitro derived precursor to the hematopoietic stem cell (HSC) with limited engrafting ability in transplanted mice, but with multipotent hematopoietic potential. Because this protocol efficiently expands the pre-blood precursors and hematopoietic progenitors, it is ideal for testing novel factors for the generation and expansion of definitive HSCs with long-term repopulating ability.